General

Guideline Title

Patient blood management guidelines: module 2 - perioperative.

Bibliographic Source(s)

National Blood Authority. Patient blood management guidelines: module 2 - perioperative. Canberra ACT (Australia): National Blood Authority; 2012. 168 p. [325 references]

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Definitions for the levels of evidence (I, II, III-1, III-2, III-3, IV) and grades of recommendations (A-D, Practice Point) are provided at the end of the "Major Recommendations" field.

Patient Blood Management Program

Establishment

Health-care services should establish a multidisciplinary, multimodal perioperative patient blood management program (Grade C). This should include preoperative optimisation of red cell mass and coagulation status; minimisation of perioperative blood loss, including meticulous attention to surgical haemostasis; and tolerance of postoperative anaemia.

Implementation

To implement the above recommendations, a multimodal, multidisciplinary patient blood management program is required. All surgical patients should be evaluated as early as possible to coordinate scheduling of surgery with optimisation of the patient's haemoglobin and iron stores (Practice Point).

Procedural Guidelines

Acute normovolaemic haemodilution (ANH) requires a local procedural guideline that addresses patient selection, vascular access, volume of blood withdrawn, choice of replacement fluid, blood storage and handling, and timing of reinfusion (Practice Point).

Intraoperative cell salvage requires a local procedural guideline that should include patient selection, use of equipment and reinfusion. All staff operating cell salvage devices should receive appropriate training, to ensure knowledge of the technique and proficiency in using it (Practice Point).

Anaemia and Haemostasis Management

Preoperative Anaemia Assessment

In patients undergoing cardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise red blood cell (RBC) transfusion, which may be associated with an increased risk of morbidity, mortality, intensive care unit (ICU) length of stay and hospital length of stay (Grade C).

In patients undergoing noncardiac surgery, preoperative anaemia should be identified, evaluated and managed to minimise RBC transfusion, which may be associated with an increased risk of morbidity, mortality, ICU length of stay and hospital length of stay (Grade C).

To implement the above recommendations, a multimodal, multidisciplinary patient blood management program is required. All surgical patients should be evaluated as early as possible to coordinate scheduling of surgery with optimisation of the patient's haemoglobin and iron stores (Practice Point).

All surgical patients should be evaluated as early as possible to manage and optimise haemoglobin and iron stores (Practice Point).

Elective surgery should be scheduled to allow optimisation of patients' haemoglobin and iron stores (Practice Point).

Iron and Erythropoiesis-Stimulating Agents (ESAs)

In surgical patients with, or at risk of, iron-deficiency anaemia, preoperative oral iron therapy is recommended (Grade B). Refer to the preoperative haemoglobin assessment and optimisation template (Appendix F in the original guideline document) for further information on the optimal dosing strategy.

In patients with preoperative anaemia, where an ESA is indicated, it must be combined with iron therapy (Grade A).

In patients with postoperative anaemia, early oral iron therapy is not clinically effective; its routine use in this setting is not recommended (Grade B).

Surgical patients with suboptimal iron stores (as defined by a ferritin level <100 µg/L) in whom substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, should be treated with preoperative iron therapy (Practice Point). Refer to the preoperative haemoglobin assessment and optimisation template (Appendix F in the original guideline document) for further information on the evaluation and management of preoperative patients.

In patients with preoperative iron-deficiency anaemia or depleted iron stores, treatment should be with iron alone. In patients with anaemia of chronic disease (also known as anaemia of inflammation), ESAs may be indicated (Practice Point). Refer to the preoperative haemoglobin assessment and optimisation template (Appendix F in the original guideline) for further information on the evaluation and management of preoperative patients.

Haemostasis Management

In patients undergoing coronary artery bypass grafting (CABG) either with or without cardiopulmonary bypass surgery (CPB) (off-pump coronary artery bypass [OPCAB]), clopidogrel therapy should be stopped, where possible, at least 5 days before surgery (Grade C).

In patients undergoing noncardiac surgery, it is reasonable to continue low dose aspirin therapy. This may require specific evaluation in neurosurgery and intraocular surgery (Grade C).

In patients undergoing elective orthopaedic surgery, nonsteroidal anti-inflammatory drug (NSAID) therapy should be ceased preoperatively to reduce blood loss and transfusion (Grade C). The timing of the cessation should reflect the agent's pharmacology.

In patients undergoing minor dental procedures, arthrocentesis, cataract surgery, upper gastrointestinal endoscopy without biopsy or colonoscopy without biopsy, warfarin may be continued (Grade B).

In patients undergoing cardiac surgery, aspirin may be continued until the time of surgery (Practice Point).

In patients receiving clopidogrel who are scheduled for elective noncardiac surgery or other invasive procedures, a multidisciplinary approach should be used to decide whether to cease therapy or defer surgery, balancing the risk of bleeding and thrombotic events. Specific evaluation is required for patients who had a recent stroke, or received a drug-eluting stent within the last 12 months or a bare metal stent within the last 6 weeks. If a decision is made to cease therapy preoperatively, this should occur 7 to 10 days before surgery (Practice Point).

In patients receiving warfarin who are scheduled for elective noncardiac surgery or other invasive procedures (excluding minor procedures—see recommendation above), specific management according to current guidelines is required (e.g., guidelines from the American College of Chest Physicians and the Australasian Society of Thrombosis and Haemostasis) (Practice Point).

Blood Conservation Strategies

Preoperative

Preoperative Autologous Donation (PAD)

The *routine* use of PAD is not recommended because, although it reduces the risk of allogeneic RBC transfusion, it increases the risk of receiving any RBC transfusion (allogeneic and autologous) (Grade C).

Intraoperative

Prevention of Hypothermia

In patients undergoing surgery, measures to prevent hypothermia should be used (Grade A).

Appropriate Patient Positioning

Excessive venous pressure at the site of surgery should be avoided by appropriate patient positioning, both during and after the procedure (Practice Point).

Deliberate Induced Hypotension

In patients undergoing radical prostatectomy or major joint replacement, if substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, deliberate induced hypotension (mean arterial blood pressure [MAP] 50–60 mmHg) should be considered, balancing the risk of blood loss and the preservation of vital organ perfusion (Grade C).

Acute Normovolaemic Haemodilution (ANH)

In adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, the use of ANH should be considered (Grade C).

ANH requires a local procedural guideline that addresses patient selection, vascular access, volume of blood withdrawn, choice of replacement fluid, blood storage and handling, and timing of reinfusion (Practice Point).

Intraoperative Cell Salvage

In adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, intraoperative cell salvage is recommended (Grade C).

Intraoperative cell salvage requires a local procedural guideline that should include patient selection, use of equipment and reinfusion. All staff operating cell salvage devices should receive appropriate training, to ensure knowledge of the technique and proficiency in using it (Practice Point).

Haemostasis Analysis

In adult patients undergoing cardiac surgery, the use of thromboelastography (TEG) should be considered (Grade C).

Medications

Aprotinin

There is evidence for the beneficial effect of intravenous aprotinin on incidence and volume of transfusion, blood loss, and the risk of reoperation for bleeding. However, the drug has been withdrawn due to concerns that it is less safe than alternative therapies[a] (Practice Point).

[a]Web sites of the:

- Therapeutic Goods Administration (www.tga.gov.au)
- MedSafe (www.medsafe.govt.nz)
- United States Food and Drug Administration (www.fda.gov)

Tranexamic Acid

In adult patients undergoing cardiac surgery, the use of intravenous tranexamic acid is recommended (Grade A).

In adult patients undergoing noncardiac surgery, if substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, the use of intravenous tranexamic acid is recommended (Grade B).

ε-Aminocaproic Acid

In adult patients undergoing cardiac surgery, the use of intravenous ε-aminocaproic acid is recommended (Grade C).

There is evidence for the beneficial effect of intravenous ε-aminocaproic acid on reduction of perioperative blood loss and volume of transfusion (Grade C). However, the drug is not marketed in Australia and New Zealand (Practice Point).

Desmopressin

In adult patients undergoing surgery in which substantial blood loss (blood loss of a volume great enough to induce anaemia that would require therapy) is anticipated, the *routine* use of desmopressin is not supported, due to uncertainty about the risk of stroke and mortality (Practice Point).

Postoperative

Postoperative Cell Salvage

In adult patients undergoing cardiac surgery or total knee arthroplasty, in whom significant postoperative blood loss is anticipated, postoperative cell salvage should be considered (Grade C).

Appropriate Transfusion Practices

Triggers for Blood Component Transfusion

RBC transfusion should not be dictated by a haemoglobin 'trigger' alone, but should be based on assessment of the patient's clinical status. In the absence of acute myocardial or cerebrovascular ischaemia, postoperative transfusion may be inappropriate for patients with a haemoglobin level of >80 g/L (Practice Point).

Patients should not receive a transfusion when the haemoglobin level is ≥100 g/L. In postoperative patients with acute myocardial or cerebrovascular ischaemia and a haemoglobin level of 70–100 g/L, transfusion of a single unit of RBC, followed by reassessment of clinical efficacy, is appropriate (Practice Point).

In general, patients with a platelet count $\geq 50 \times 10^9$/L *or* an international normalised ratio (INR) ≤2 can undergo invasive procedures without any serious bleeding; however, lower platelet counts and higher INRs may be tolerated (Practice Point).

Specialist guidelines or haematology advice should be sought for at-risk patients undergoing intracranial, intraocular and neuraxial procedures, and for patients with severe thrombocytopenia or coagulopathy (Practice Point).

Fresh Frozen Plasma (FFP)

The prophylactic use of FFP in cardiac surgery is not recommended (Grade B).

Platelets

The prophylactic use of platelets after cardiac surgery is not supported (Practice Point).

Recombinant Activated Factor VII (rFVIIa)

The prophylactic or routine therapeutic use of rFVIIa is not recommended because concerns remain about its safety profile, particularly in relation to thrombotic adverse events (Grade C).

The administration of rFVIIa may be considered in the perioperative patient with life-threatening haemorrhage after conventional measures, including surgical haemostasis, use of antifibrinolytics and appropriate blood component therapy have failed (Practice Point).

Definitions

National Health and Medical Research Council (NHMRC) Evidence Hierarchy: Designations of Levels of Evidence According to Type of

Research Question*

Level	Intervention[a]	Prognosis	Aetiology[b]
I[c]	A systematic review of Level II studies	A systematic review of Level II studies	A systematic review of Level II studies
II	A randomised controlled trial (RCT)	A prospective cohort study[d]	A prospective cohort study
III-1	A pseudo RCT (i.e., alternate allocation or some other method)	All or none[e]	All or none[e]
III-2	A comparative study with concurrent controls: • Non-randomised, experimental trial[f] • Cohort study • Case–control study • Interrupted time series with a control group	Analysis of prognostic factors amongst persons in a single arm of a RCT	A retrospective cohort study
III-3	A comparative study without concurrent controls: • Historical control study • Two or more single arm study[g] • Interrupted time series without a parallel control group	A retrospective cohort study	A case–control study
IV	Case series with either post-test or pre-test/post-test outcomes	Case series, or cohort study of persons at different stages of disease	A cross-sectional study or case series

*Source: National Health and Medical Research Council (NHMRC) (2009). NHMRC additional levels of evidence and grades for recommendations for developers of guidelines. NHMRC. https://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/developers/nhmrc_levels_grades_evidence_120423.pdf

[a]Definitions of these study designs are provided on pages 7-8, *How to use the evidence: assessment and application of scientific evidence* (NHMRC, 2000).

[b]If it is possible and ethical to determine a causal relationship using experimental evidence, then the 'intervention' hierarchy of evidence should be utilised. If it is only possible or ethical to determine a causal relationship using observational evidence (e.g., groups cannot be allocated to a potential harmful exposure, such as nuclear radiation), then the 'aetiology' hierarchy of evidence should be utilised.

[c]A systematic review will only be assigned a level of evidence as high as the studies it contains, except where those studies contain Level II evidence. Systematic reviews of Level II evidence provide more data than the individual studies, and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review quality should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome or result, as different studies (and study designs) might contribute to each different outcome.

[d]At study inception, the cohort is either non-diseased or all at the same stage of the disease. A randomised controlled trial with persons either non-diseased or at the same stage of the disease in both arms of the trial would also meet the criterion for this level of evidence.

[e]All or none of the people with the risk factor(s) experience the outcome; and the data arises from an unselected or representative case series which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and

clear proof of the causal link has come from the disappearance of smallpox after large-scale vaccination.

[f]This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (i.e., utilise A vs. B and B vs. C to determine A vs. C).

[g]Comparing single arm studies, i.e., case series from two studies. This would also include unadjusted indirect comparisons (i.e., utilise A vs. B and B vs. C to determine A vs. C, without statistical adjustment for B).

Body of Evidence Matrix

Component	A	B	C	D
	Excellent	Good	Satisfactory	Poor
Evidence Base	Several Level I or II studies with low risk of bias	One or two Level II studies with low risk of bias or a systematic review, or multiple Level III studies with low risk of bias	Level III studies with low risk of bias, or Level I or II studies with moderate risk of bias	Level IV studies, or Level I to III studies with high risk of bias
Consistency	All studies consistent	Most studies consistent and inconsistency can be explained	Some inconsistency reflecting genuine uncertainty around clinical question	Evidence is inconsistent
Clinical Impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population/s studied in body of evidence are the same as the target population for the guideline	Population/s studied in the body of evidence are similar to the target population for the guideline	Population/s studied in the body of evidence are different to the target population but it is clinically sensible to apply this evidence to the target population for the guidelines	Population/s studied in the body of evidence are different to the target population, and it is hard to judge whether it is sensible to generalise to the target population for the guidelines
Applicability	Directly applicable to the Australian healthcare context	Applicable to Australian healthcare context, with a few caveats	Probably applicable to Australian healthcare context with some caveats	Not applicable to the Australian healthcare context

Grade of Recommendation

Grade A: Body of evidence can be trusted to guide practice.

Grade B: Body of evidence can be trusted to guide practice in most situations.

Grade C: Body of evidence provides some support for recommendation(s) but care should be taken in its application.

Grade D: Body of evidence is weak and recommendations must be applied with caution.

Practice Point: The systematic review found insufficient high-quality data to produce evidence-based recommendations, but the CRG felt that clinicians require guidance to ensure good clinical practice.

Clinical Algorithm(s)

An algorithm titled "Preoperative Haemoglobin Assessment and Optimisation Template" is provided in the original guideline document.

Scope

Disease/Condition(s)

Anticipated blood loss associated with surgery or invasive procedures

Guideline Category

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Anesthesiology

Critical Care

Emergency Medicine

Hematology

Surgery

Intended Users

Advanced Practice Nurses

Hospitals

Nurses

Physician Assistants

Physicians

Guideline Objective(s)

- To inform health-care practitioners, health educators, and health service managers and policy makers about the pre-, intra- and postoperative care of patients undergoing surgery or invasive procedures, particularly those in which blood loss is anticipated
- To support the introduction of patient blood management practices in the perioperative setting

Target Population

Patients undergoing surgical and invasive procedures

Interventions and Practices Considered

1. Establishing and implementing a multidisciplinary, multimodal perioperative patient blood management program
    - Establishing local procedural guideline for acute normovolaemic haemodilution (ANH)

    - Establishing local procedural guideline for intraoperative cell salvage
2. Anaemia and haemostasis management
    - Preoperative anaemia assessment
    - Use of preoperative iron and erythropoiesis-stimulating agents (ESAs)
    - Stopping or continuing clopidogrel, low-dose aspirin, nonsteroidal anti-inflammatory drugs (NSAIDs), or warfarin based on type of surgery and risk of bleeding and thrombotic events
3. Blood conservation strategies
    - Preoperative autologous donation (PAD) (not recommended routinely)
    - Prevention of hypothermia intraoperatively
    - Appropriate patient positioning
    - Deliberate induced hypotension
    - Use of ANH
    - Use of intraoperative cell salvage
    - Haemostasis analysis: use of thromboelastography (TEG)
    - Aprotinin
    - Tranexamic acid
    - ε-Aminocaproic acid
    - Desmopressin (not recommended routinely)
    - Postoperative cell salvage
4. Appropriate transfusion practices
    - Triggers for blood component transfusion
    - Prophylactic use of fresh frozen plasma (FFP) (not recommended)
    - Prophylactic use of platelets (not recommended)
    - Prophylactic or routine use of recombinant activated factor VII (rFVIIa) (not recommended)
    - Use of rFVIIa in the perioperative patient with life-threatening haemorrhage after conventional measures have failed

Major Outcomes Considered

- Mortality
- Morbidity
- Quality of life
- Transfusion frequency and dose or type of transfusion
- Blood loss
- Change in haemoglobin (Hb) (preoperative, postoperative, discharge and 28-day Hb levels)
- Length of hospital or intensive care unit stay
- Re-operation for bleeding
- Correction or prevention of disseminated intravascular coagulation (DIC) and coagulopathy
- Cost
- Hospital readmission

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The clinical research questions for systematic review were structured according to PICO ('population, intervention, comparator and outcome' for intervention questions), PPO ('population, predictor and outcome' for prognostic questions) or PRO ('population, risk factor and outcome' for aetiology questions) criteria. Three main strategies were used to identify potentially relevant literature: electronic database searching, manual searching and use of literature recommended by expert members of the Clinical/Consumer Reference Group (CRG).

The primary databases searched were EMBASE, Medline, the Cochrane Library Database and PreMedline. Additional searches were conducted of Cumulative Index to Nursing and Allied Health Literature and Australasian Medical Index. The electronic searches included articles published after 1966. Literature retrievals were limited by the holdings of the databases accessed. Publication cut-off points varied from 29 April 2009 to 30 June 2009 (see Table D.1 in the original guideline document). Any future searches undertaken to revise, reuse or update these searches should take 1 April 2009 as the start date, to ensure complete coverage of the date range.

Following a review of the search results by the CRG in November 2009, the terms for some searches (specific question 2 and generic question 6) were revised to ensure inclusion of patients undergoing invasive procedures and minimally invasive surgical procedures. Table D.1 in the original guideline document shows the dates on which the revised searches were conducted. The cut-off date for these searches was 30 June 2009, to better align with previous cut-off dates.

Inclusion criteria were determined from the PICO, PPO or PRO criteria that formed the basis of the systematically reviewed research questions. Non-English publications were excluded.

See the Technical Reports accompanying these guidelines for further details on search strategies and inclusion criteria (see the "Availability of Companion Documents" field).

Number of Source Documents

See Appendix C in Technical Report volume 2a (see the "Availability of Companion Documents" field) for diagrams depicting literature search results and included studies for all review questions except question 3. For review question 3, see Appendix C in Technical Report volume 2b (see the "Availability of Companion Documents" field) for full literature search results.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

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III-3 Level	A comparative study without concurrent controls: Intervention[a]	A retrospective cohort study Prognosis	A case–control study Aetiology[b]
	• Historical control study • Two or more single arm study[g] • Interrupted time series without a parallel control group		
IV	Case series with either post-test or pre-test/post-test outcomes	Case series, or cohort study of persons at different stages of disease	A cross-sectional study or case series

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[c]A systematic review will only be assigned a level of evidence as high as the studies it contains, except where those studies contain Level II evidence. Systematic reviews of Level II evidence provide more data than the individual studies, and any meta-analyses will increase the precision of the overall results, reducing the likelihood that the results are affected by chance. Systematic reviews of lower level evidence present results of likely poor internal validity and thus are rated on the likelihood that the results have been affected by bias, rather than whether the systematic review itself is of good quality. Systematic review quality should be assessed separately. A systematic review should consist of at least two studies. In systematic reviews that include different study designs, the overall level of evidence should relate to each individual outcome or result, as different studies (and study designs) might contribute to each different outcome.

[d]At study inception, the cohort is either non-diseased or all at the same stage of the disease. A randomised controlled trial with persons either non-diseased or at the same stage of the disease in both arms of the trial would also meet the criterion for this level of evidence.

[e]All or none of the people with the risk factor(s) experience the outcome; and the data arises from an unselected or representative case series which provides an unbiased representation of the prognostic effect. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of smallpox after large-scale vaccination.

[f]This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (i.e., utilise A vs. B and B vs. C to determine A vs. C).

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Body of Evidence Matrix

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Component	A	B	C	D
Consistency	All studies consistent Excellent	Most studies consistent and inconsistency can be explained Good	Some inconsistency reflecting genuine uncertainty around clinical question Satisfactory	Evidence is inconsistent Poor
Clinical Impact	Very large	Substantial	Moderate	Slight or restricted
Generalisability	Population/s studied in body of evidence are the same as the target population for the guideline	Population/s studied in the body of evidence are similar to the target population for the guideline	Population/s studied in the body of evidence are different to the target population but it is clinically sensible to apply this evidence to the target population for the guidelinesc	Population/s studied in the body of evidence are different to the target population, and it is hard to judge whether it is sensible to generalise to the target population for the guidelines
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Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Systematic reviews were undertaken to attempt to answer the questions specific to perioperative transfusion, and the generic questions relevant to all six modules of the Patient Blood Management Guidelines. The systematic review questions are listed in Box 2.1 in the original guideline document. Refer to the Technical Reports (see the "Availability of Companion Documents" field) for details concerning the systematic review process and all evidence summary tables.

Classification and Assessment of Evidence

Studies identified for inclusion from the literature search were classified according to the National Health and Medical Research Council (NHMRC) levels of evidence hierarchy (see the "Rating Scheme for the Strength of the Evidence" field). To ensure that modules were based on the best available evidence, studies of higher levels of evidence (Levels I or II) were included in preference to those presenting lower levels of evidence (Levels III or IV). This was to minimise the potential for bias in the evidence base for each systematically reviewed question. However, lower level studies were reviewed where evidence was not available in higher level studies for any of the primary outcomes.

Studies identified from the systematic literature review were assessed according to NHMRC dimensions of evidence (see Table 2.4.2 in Technical Report Volume 1a). There are three main domains: strength of the evidence, size of the effect, and relevance of the evidence. The first domain was derived directly from the literature identified for a particular intervention, aetiology or prognostic study. The other two domains were determined in consultation with the Clinical/Consumer Reference Group (CRG) as part of the study assessment process during the review of the evidence considered for module development. An aspect of the strength of the evidence domain is the level of evidence of the study, which was determined as described above using the NHMRC levels of evidence hierarchy.

Quality Appraisal

The methodological quality of the included studies was assessed using the criteria presented in Appendix 3 of Technical Report Volume 1a. Quality assessment criteria varied according to whether included studies were systematic reviews, randomised controlled trials (RCTs), cohort studies or case–control studies. No weighting of quality criteria was applied, but studies that met all criteria, or all but one, were considered good quality with a low risk of bias. Quality assessments of included studies for all systematically reviewed research questions are presented in Appendix E of Technical Report Volume 2a.

Data Extraction

Data and information were extracted into evidence summary tables according to the inclusion criteria (population, intervention, comparator, outcome [PICO], population, risk, outcome [PRO] or population, predictor, outcome [PPO]). Evidence summary tables were based on NHMRC requirements for externally developed guidelines. Extracted data and information included general study details (citation, study design, evidence level, country and setting), characteristics of study participants, details of interventions and comparators, details of internal (e.g., allocation and blinding) and external (applicability and generalisability) study validity; and results for outcomes specified in the inclusion criteria. Where relevant studies were identified, extracted data and information were used to construct study characteristics and results tables of included evidence for each systematically reviewed research question.

Assessment of the Body of Evidence

The body of evidence for each module recommendation was graded in accordance with the NHMRC framework for developing evidence-based recommendations. Assessment of the body of evidence considers the dimensions of evidence of studies relevant to that recommendation. The NHMRC developed an evidence statement form to be used with each clinical research question considered in guidelines development (see Appendix 3 of Technical Report Volume 1a). Before the evidence statement form was completed, included studies were critically appraised and relevant data were summarised, as described. This information was required to formulate each recommendation and determine the overall grade of the body of evidence supporting each recommendation.

The key findings from included studies were summarised as evidence statements for each systematically reviewed research question. Where required, separate evidence statements were developed for different patient populations and outcomes. CRG input helped ensure that the size of effects and relevance of evidence were considered when developing evidence statements. Where no evidence or insufficient relevant evidence was identified, this was explained in the evidence statement.

Refer to Technical Report Volume 1a for Steps 1 and 2 in using the NHMRC evidence statement form.

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

The Clinical/Consumer Reference Group (CRG) developed recommendations where sufficient evidence was available from the systematic review of the literature. The recommendations have been carefully worded to reflect the strength of the body of evidence. Each recommendation has been given a grade, which were set by the National Health and Medical Research Council (NHMRC) (see section 2 in the original guideline document for further information on this process).

Governance Structure

A multilevel management framework was established by the NBA to coordinate the development of the new patient blood management guidelines. The management framework (illustrated in Appendix A of the original guideline document) consists of:

- A Steering Committee, responsible for the overall development and governance of the entire project
- An Expert Working Group (EWG), responsible for clinical oversight and integration of the six modules
- Clinical/Consumer Reference Groups (CRGs – one for each of the six modules), with membership including representation from relevant colleges, societies and consumer groups, to provide expert knowledge and input
- Systematic reviewers and a technical writer, contracted by the NBA to review the literature and develop a draft of each module
- Guidelines Assessment Register (GAR) consultants, to provide advice and mentoring to the systematic reviewers, technical writer, EWG and CRGs; and to ensure that the development process and the guidelines produced comply with National Health and Medical Research Council (NHMRC) requirements.

The NBA provided the secretariat, project funding and project management. The NBA Web site includes a list of colleges and societies that have endorsed these guidelines. Appendix A in the original guideline document lists the membership of the bodies involved in governance of the guidelines. Details of how the guidelines will be implemented and updated are provided in Chapter 6 of the guideline.

Formulation of Recommendations

Use of the NHMRC Evidence Statement Form

Step 3: Formulation of a Recommendation Based on the Body of Evidence

Step 3 involved formulating the wording of the recommendation. This wording was intended to reflect the strength of the body evidence; that is, where the evidence base was regarded as poor or unreliable, words such as 'must' or 'should' were not used. The wording of recommendations was developed in conjunction with the CRG during meetings to review the evidence base for research questions.

Step 4: Determination of the Grade for the Recommendation

The overall grade for each recommendation was determined from a summary of the rating for each component of the body of evidence (outlined in the "Rating Scheme for the Strength of the Evidence" field). Definitions of the NHMRC grades of recommendations are presented in the "Rating Scheme for the Strength of the Recommendations" field. In accordance with the NHMRC framework, recommendations were not graded A or B unless the evidence base and consistency of evidence were both rated A or B unless only one study was included and consistency was rated 'N/A'. In this situation the quality, size and strength of the evidence base was relied upon to grade the recommendation. The grading of recommendations was determined in conjunction with the CRG.

Developed recommendations were entered into the NHMRC evidence statement forms to accompany the corresponding evidence statement matrix, along with the overall grade determined in this step (see Appendix D of Technical Report Volume 2a [see the "Availability of Companion Documents" field]).

Practice Points

Practice points were developed by the CRG through a facilitated group discussion (see Appendix 4 in Technical Report Volume 1a [see the "Availability of Companion Documents" field]) in the following circumstances:

- Where the underpinning evidence would have led to a grade D evidence-based recommendation
- Where the CRG developed evidence-based recommendations graded C and above, but considered that additional information was required to guide clinical practice. Wherever possible, this guidance was sourced from other evidence-based guidelines assessed to be of high quality
- Where insufficient evidence was identified to support the development of an evidence-based recommendation

Rating Scheme for the Strength of the Recommendations

Grade of Recommendation

Grade A: Body of evidence can be trusted to guide practice.

Grade B: Body of evidence can be trusted to guide practice in most situations.

Grade C: Body of evidence provides some support for recommendation(s) but care should be taken in its application.

Grade D: Body of evidence is weak and recommendations must be applied with caution.

Practice Point: The systematic review found insufficient high-quality data to produce evidence-based recommendations, but the Clinical/Consumer Reference Group (CRG) felt that clinicians require guidance to ensure good clinical practice.

Cost Analysis

The cost-effectiveness evidence for all review questions is summarised in the technical reports accompanying the guideline (see the "Availability of Companion Documents" field).

Method of Guideline Validation

External Peer Review

Description of Method of Guideline Validation

Public Consultation

Public consultation was conducted for eight weeks, from 7 February 2011, during which time the draft module was available on the National Blood Authority (NBA) Web site. Notification was posted in *The Australian* national newspaper, and the NBA invited a range of stakeholders, committees, working groups and interested people to provide submissions.

Twenty-five submissions were received. The Clinical/Consumer Reference Group (CRG) met on 9-10 May and 12-13 July to consider all responses to the public consultation submissions and, where necessary, revise this module in accordance with the submissions. Many changes were made to the module, to address comments and concerns raised in submissions, and to improve clarity.

Finalising the Guidelines

The final drafts of the module and technical reports were reviewed by a guidelines development expert (formerly a Guidelines Assessment Registrar [GAR] consultant) to assess compliance with National Health and Medical Research Council (NHMRC) requirements for externally developed guidelines. The module was then reviewed by an Appraisal of Guidelines for Research and Evaluation (AGREE) II expert to assess it against international quality standards. The module and accompanying documents were then sent to the NHMRC for methodological and independent peer review on 4 August 2011.

The module was further refined in response to the reviewer's recommendations. Approval from the NHMRC was received on 15 November 2011.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is identified and graded for each recommendation (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Improvement of clinical outcomes by avoiding unnecessary exposure to blood components including:

- Optimisation of blood volume and red cell mass
- Minimisation of blood loss
- Optimisation of the patient's tolerance of anaemia

Potential Harms

Traditionally, it has been assumed that blood transfusion benefits patients; however, a benefit has not been demonstrable in many clinical scenarios. In addition, evidence is accumulating that transfusion-related acute lung injury is more common than previously thought, and that more recently identified conditions – including transfusion-related immunomodulation – may cause patients harm.

The risk of transmission of infectious diseases has reduced significantly in recent years through improved manufacturing and laboratory processes. Nevertheless, there is still a small potential for transfusion of an unrecognised infectious agent.

Despite improvements in systems management, there remains a risk of transfusion-related harm due to administrative error. Such an error has the potential to result in acute haemolytic reaction from ABO incompatibility, which may be fatal.

Of the recognised adverse events associated with transfusion, the most common is transfusion-associated circulatory overload, which is reported in up to 1% of patients receiving transfusions.

The clinical decision to undertake transfusion therapy should only be made after full consideration of the risks and benefits. Table B.1 in the original guideline document summarises the risks and benefits; Table B.2 puts the risks into perspective; and Table B.3 presents the Calman chart (United

Kingdom risk per one year), which may be useful to clinicians for explaining risks to patients.

Qualifying Statements

Qualifying Statements

- This document is a general guide to appropriate practice, to be followed subject to the circumstances, clinician's judgement and patient's preferences in each individual case. It is designed to provide information to assist decision making. Recommendations contained herein are based on the best available evidence published up to the dates shown in Appendix D in the original guideline document. The relevance and appropriateness of the information and recommendations in this document depend on the individual circumstances. Moreover, the recommendations and guidelines are subject to change over time.
- Each of the parties involved in developing this document expressly disclaims and accepts no responsibility for any undesirable consequences arising from relying on the information or recommendations contained herein.
- This publication reflects the views of the authors and not necessarily the views of the Australian Government.
- The information in the guideline algorithm, developed by consensus, can be used as a guide. Any algorithm should always take into account the patient's history and clinical assessment, and the nature of the proposed surgical procedure.
- Transfusion decisions for patients should take into account each individual's clinical circumstances and physiological status, and their treatment preferences and choices.
- If blood components are likely to be indicated, transfusion should not be a default decision. Instead, the decision on whether to transfuse should be carefully considered, taking into account the full range of available therapies, and balancing the evidence for efficacy and improved clinical outcome against the potential risks.

Implementation of the Guideline

Description of Implementation Strategy

Implementing, Evaluating and Maintaining the Guidelines

The National Blood Authority (NBA), in collaboration with the Steering Committee and Expert Working Group (EWG) members, developed a plan to guide appropriate communication on the implementation of this module. The plan identifies target audiences for the module, strategies and tools for effective implementation, communication channels and key messages. Continued re-evaluation of the guidelines is necessary to reduce variation in practice patterns, support appropriate use of blood component therapy and reduce inappropriate exposure of patients to blood components. A plan was designed to evaluate implementation of the six modules of the guidelines and to determine:

- The extent to which the guidelines influence changes in clinical practice and health outcomes
- What factors (if any) contribute to noncompliance with the guidelines

The results of the evaluation will be used to inform future review of the guidelines. Economic issues were considered when formulating the evidence-based recommendations, and the recommendations will have cost implications. Savings are expected to be derived from reduced use of product and an associated reduction in hospital and laboratory costs. However, the Clinical/Consumer Reference Group (CRG) anticipates that additional costs will be incurred due to the system re-design and training associated with wider implementation of preoperative anaemia assessment and treatment, improved collection and use of data to inform practice, introduction of new surgical techniques and wider uptake of other technologies such as cell salvage. While economic models have indicated a net benefit from the implementation of patient blood management practices, no economic model has been developed for the Australian setting. The NBA, together with the Jurisdictional Blood Committee (JBC) and key stakeholders, is developing a program to facilitate uptake of the guidelines that take into account the challenges raised in Section 5.2 of the original guideline document. A number of initiatives have commenced, including initial investment in the development of a patient blood management toolkit that will help jurisdictions and individual hospitals to implement patient blood management practices. Patient blood management content has been included in nationally available education programs such as the BloodSafe eLearning Program and the Post Graduate Certificate in Transfusion Practice that is available through the University of Melbourne. Also under development is a national data dictionary that will facilitate data linkage and thus support jurisdictional evaluation of appropriate use of red cells.

Implementation of Guidelines Recommendations

The National Health and Medical Research Council (HMRC) framework directs that guidelines implementation should be considered at the same time that recommendations are formulated. The NHMRC evidence statement form contains questions related to the implementation of each module (see Appendix 3 in Technical Report Volume 1a [see the "Availability of Companion Documents" field]). These are:

- Will this recommendation result in changes in usual care?
- Are there any resource implications associated with implementing this recommendation?
- Will the implementation of this recommendation require changes in the way care is currently organised?
- Is the guidelines development group aware of any barriers to the implementation of this recommendation?

This section of the NHMRC evidence statement form was completed in consultation with the CRG when each recommendation was formulated and graded. Implementation issues are recorded in the NHMRC evidence statement forms presented in Appendix D of Technical Report Volume 2a (see the "Availability of Companion Documents" field).

Implementation Tools

Audit Criteria/Indicators

Clinical Algorithm

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

Resources

Staff Training/Competency Material

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Safety

Timeliness

Identifying Information and Availability

Bibliographic Source(s)

National Blood Authority. Patient blood management guidelines: module 2 - perioperative. Canberra ACT (Australia): National Blood Authority; 2012. 168 p. [325 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2012

Guideline Developer(s)

National Blood Authority - National Government Agency [Non-U.S.]

Source(s) of Funding

Funding, Secretariat and Project Management was provided by the National Blood Authority Australia. The systematic review methods, writing of the document or development of the final recommendations and practice points have not been influenced by the views or interests of the funding body.

Guideline Committee

Steering Committee

Expert Working Group

Clinical/Consumer Reference Group (CRG) - Perioperative

Composition of Group That Authored the Guideline

Steering Committee: Dr Alison Turner (*Chair*), National Blood Authority; Dr Heather Buchan, National Institute of Clinical Studies; Ms Cathy Clutton, National Health and Medical Research Council; Ms Vesna Cvjeticanin, National Health and Medical Research Council; Mr Ken Davis, Australian & New Zealand Society of Blood Transfusion; Prof Henry Ekert, Australian Government Department of Health & Ageing; Ms Sue Ireland, Jurisdictional Blood Committee; Dr Amanda Thomson, Australian & New Zealand Society of Blood Transfusion

Expert Working Group: Dr Craig French (*Co-chair*), College of Intensive Care Medicine of Australia and New Zealand, and Australian & New Zealand Intensive Care Society; Dr Amanda Thomson (*Co-chair*), Australian & New Zealand Society of Blood Transfusion; A/Prof Donald Bowden, Thalassaemia Australia; A/Prof Mark Dean, Haematology Society of Australia and New Zealand & Royal Australasian College of Physicians; Mr Shannon Farmer, Independent consumer advocate; Dr Chris Hogan, National Blood Authority; Ms Janine Learmont, Royal College of Nursing, Australia; Dr Helen Liley, Royal Australasian College of Physicians, Paediatric & Child Health Division; Dr Robert Lindeman, Royal College of Pathologists of Australasia; A/Prof Larry McNicol, Australian & New Zealand College of Anaesthetists; Prof John Olynyk, University of Western Australia Department of Medicine, Fremantle Hospital; Prof Michael Permezel, Royal Australian & New Zealand College of Obstetricians and Gynaecologists; Dr Kathryn Robinson, Australian Red Cross Blood Service; Dr Helen Savoia, Royal College of Pathologists of Australasia; Dr Richard Seigne, Australian & New Zealand Society of Blood Transfusion; Dr Philip Truskett, Royal Australasian College of Surgeons; Dr John Vinen, Australasian College for Emergency Medicine

Clinical/Consumer Reference Group for Phase 1: Prof Larry McNicol (*Chair*), Anaesthetist Australian & New Zealand College of Anaesthetist; Prof Zsolt Balogh, Trauma surgeon Royal Australasian College of Surgeon; Mr Shannon Farmer, Consumer Independent consumer advocate; Dr Craig French, Intensive care physician, College of Intensive Care Medicine of Australia and New Zealand, and Australian & New Zealand Intensive Care Society; Prof Russell Gruen, Trauma Surgeon, Royal Australasian College of Surgeons; Dr Chris Hogan, Haematologist

National Blood Authority; Dr Richard Seigne, Anaesthetist, Australian & New Zealand Society of Blood Transfusion; Mr Daryl Teague, Orthopaedic surgeon Australian Orthopaedic Association; Dr Amanda Thomson, Haematologist, Australian & New Zealand Society of Blood Transfusion; Dr Philip Truskett, Surgeon, Royal Australasian College of Surgeons; Dr John Vinen, Emergency Physician, Australasian College for Emergency Medicine

Financial Disclosures/Conflicts of Interest

All members of the Steering Committee, Clinical/Consumer Reference Group (CRG) and Expert Working Group (EWG) declared any conflicts of interest before starting work on the guideline. Conflicts of interest were also reviewed at intervals, and were required to be declared at the start of each meeting. No conflicts of interest were declared, by any Steering Committee, CRG or EWG member, during the development of the Patient Blood Management Guidelines: Module 2 Perioperative.

Guideline Endorser(s)

Australasian College for Emergency Medicine - Medical Specialty Society

Australasian Society for Emergency Medicine - Medical Specialty Society

Australian & New Zealand Intensive Care Society - Nonprofit Organization

Australian and New Zealand College of Anaesthetists - Medical Specialty Society

Australian College of Nursing - Professional Association

College of Intensive Care Medicine of Australia and New Zealand - Medical Specialty Society

Medical Oncology Group of Australia - Professional Association

Perinatal Society of Australia and New Zealand - Medical Specialty Society

Royal Australasian College of Surgeons - Professional Association

Royal Australian and New Zealand College of Obstetricians and Gynaecologists - Professional Association

Royal College of Pathologists of Australasia - Professional Association

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Blood Authority (NBA) Web site .

Availability of Companion Documents

The following are available:

- Patient blood management guidelines: module 2 - perioperative. Quick reference guide. Canberra ACT (Australia): National Blood Authority; 2012. 20 p. Available from the National Blood Authority (NBA) Web site .
- Patient blood management guidelines: module 2 - perioperative. Technical report. Volume 1a. Review of the evidence (questions 1,2 and 4-9). Canberra ACT (Australia): National Blood Authority; 2011 Jul. 286 p. Available from the NBA Web site .
- Patient blood management guidelines: module 2 - perioperative. Technical report. Volume 1b. Review of evidence (question 3). Canberra

ACT (Australia): National Blood Authority; 2011 Jul. 239 p. Available from the NBA Web site.

- Patient blood management guidelines: module 2 - perioperative. Technical report. Volume 2a. Appendixes (questions 1,2 and 4-9). Canberra ACT (Australia): National Blood Authority; 2011 Jul. 792 p. Available from the NBA Web site.
- Patient blood management guidelines: module 2 - perioperative. Technical report. Volume 2b. Appendixes (question 3). Canberra ACT (Australia): National Blood Authority; 2011 Jul. 892 p. Available from the NBA Web site.

A variety of additional implementation resources, including audit tools, templates, case studies, and other guidance, are available from the NBA Web site. Instructions on how to add the guidelines to your mobile device are available from the NBA Web site.

Patient Resources

Various tools and resources to support patients in patient blood management decision making are available on the National Blood Authority (NBA) Web site.

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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